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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,491	06/15/2006	Elisabetta Bianchi	ITR0054P	4014

210 7590 02/25/2010

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EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
02/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,491	BIANCHI ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/23/09 & 8/20/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-62* is/are pending in the application.

4a) Of the above claim(s) *48-50 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-47,51,52 and 54-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *attachment*.

DETAILED ACTION

Restriction Election

1. Applicant's election of Group II, and species of Haemophilus influenza as the pathogen, sSMCC as the reagent for conjugation and OMPC as the carrier, in the reply filed on April 23, 2009, is acknowledged. Applicant's further election, with traverse, of species modification at the N-terminal and acylation of lysine, in the reply filed on August 20, 2009, is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Accordingly, Claims 37-62 are pending. Claims 48-50 and 53 are withdrawn from further consideration by the Examiner, under 37 C. F. R. 1.142(b), as being directed to a nonelected invention. Claims 37-47, 51, 52 and 54-62 are considered in this Office action.

Claim Objection

3. Claim 39 is objected to for being dependent on itself. Correction is required. For the purpose of examination, Claim 39 is assumed to depend on Claim 37.

Claim Rejections - 35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 37-47, 51, 52 and 54-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (i) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

6. The claims are indefinite because the term "peptide load" is not explicitly defined in either the claims or the specification. The term "peptide load" has been used for different meanings. For example, amyloid β peptide load apparently refers amyloid β peptide accumulation in senile plaques, see e.g. *Title* and *Introduction*; Li (PNAS, 101(10): 3632–3637, 2004). Gupata refers MHC and antigen peptide interaction and presentation as "MHC loading" or "peptide load", see e.g. Abstract and Introduction (PLoS One. 2008 Mar 19; 3(3):e1814) One of ordinary skill in the art cannot be reasonably apprised of the metes and bounds of the invention because it is not clear what "peptide load" is intended. This rejection affects all dependent claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 37-47, 51, 52 and 54-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the

sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

9. In the present case, the scope of the claims encompasses a method for making **any peptide-carrier conjugate** comprising: a) modifying a first peptide to produce a second peptide that has a lower isoelectric point (pI) than the first peptide; and b) conjugating a plurality of the second peptide to a carrier protein to obtain a peptide-carrier conjugate, **whereby the resulting peptide-carrier has increased peptide load and solubility**, in which the method requires the **second peptide has a non-naturally occurring sequence**; the second peptide has a pI that is lower than 6, wherein the second peptide has a pI that is between 2 and 6, wherein the second peptide has a pI that is between 3.5 and 5.

10. By definition, a “conjugate” means: “joined together especially in pairs” (see attached Merrian Webster). Since the claims do not define any specific peptide-carrier conjugate, the scope of the claims is extremely broad, which encompasses all possible

fused peptides or proteins of any sizes or any structures. The possible variations, in both structures and properties, are enormous for such peptide-carrier conjugates.

11. In supporting these claims, the specification has shown that 5 modified HA peptides (15-21-mers), which have lower pI than they were not modified, have increased copies of peptides conjugated to OMPC carrier, see e.g. Table II-V. However, the specification has also indicated that there are uncertainties regarding which modified peptide-carrier conjugates would have "increased peptide load and solubility" (Claim 39) "at pI 1-6, 2-6, or 3.5" (Claims 42-44), and which modified peptide-carrier conjugates would have "more than 500, or more than 100 moles of peptide/mole of carrier protein" (Claims 61 and 62). While the specification indicates that peptides having pI values between 3.5-5 favors high peptide loading to OMPC, the specification also indicates that, for higher pI values, the maximum attainable loading must be tuned to avoid precipitation of the conjugate (means have reduced solubility). For peptides that have pI values below 3.5, the maximum conjugation level of peptide chains is limited by the electrostatic repulsion effect, see e.g. [0199]. The specification [0200] has also indicated that these rules appear not to apply to those peptides with either very low or very high MW. The specification teaches that two peptides having high pI (9.5) but low MW (1100-1330 Da) could be loaded up to 3500 moles/mole OMPC. By contrast, a high MW peptide (8000 Da) could only be loaded up to 1000 moles/mole OMPC, despite a pI of about 4, see e.g. Para [0200]. Thus, the specification has shown, by testing only limited numbers of modified HA peptides, that it is not predictable *which* modified peptides would form peptide-carriers that would have increased peptide load and solubility as required by the claims.

12. Moreover, the specification lacks sufficient variety of species to reflect the variance of peptide-carrier conjugates encompassed in the scope of the claims. The specification has not shown if those tested peptides would conjugate all protein carriers, other than OMPC, resulting in increased peptide load and solubility. The specification has not shown if any peptide-any protein conjugates of different structures and sizes would result in "increased peptide load and solubility". Thus, a few HA peptide-OPMC conjugates disclosed by the specification are not representative numbers of species for all peptide-conjugates encompassed in the scope of the claims.

13. Accordingly, it is deemed that the specification fails to provide adequate written description for the claimed method of making a genus of peptide-carrier conjugates and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Remarks

14. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business

Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648